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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
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ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/798,876	UBER ET AL.	
	Examiner	Art Unit	
	MELISSA PERREIRA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-141 and 143* is/are pending in the application.

4a) Of the above claim(s) *42-139* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-41,140,141 and 143* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/9/09 has been entered.

Claims and Previous Rejection Status

2. Claims 1-4,6-41,140,141 and 143 are pending in the application. Claims 42-139 are withdrawn from consideration.

3. The rejection of claims 1-4,6-41,140,141 and143 under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Evans, III et al. (US 5,885,216) and further in view of Daum et al. (US 6,231,513) or Quay et al. (WO 96/40282) is maintained.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-4,6-41,140,141 and 143 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossling et al. (US 6,468,506B1) in view of Evans, III et al. (US 5,885,216) and in further view of Daum et al. (US 6,231,513) or Quay et al. (WO 96/40282).

6. Rossling et al. (US 6,468,506B1) discloses a system/apparatus for the production of gaseous microparticles/bubble medium for ultrasound diagnosis (i.e. imaging procedure) and the process for the production of gaseous microparticles (abstract; column 1, lines 7-12). The apparatus comprises a tank **(17)** (i.e. reservoir for storing a liquid) and may be filled with gas via a valve **(2)**, line/gas flow path **(30)** and a pump **(16)** and/or liquid gas pump **(4)** (column 5, lines 5-33). The bubble generator, having an inlet and outlet, used to create gaseous microparticles involves pumping in gas into a surface-active substance solution, applying a vacuum and mixing with a stirring mechanism (i.e. means for disrupting an interface) between the liquid and the gas, not excluding multiple small wires or disks (column 2, lines 35-53). An alternative method for the production of gaseous microparticles involves spraying the solution via a nozzle **(118)** into a column of gas where a pump **(16)** moves the solution from a tank via nozzle into a line, heat exchanger **(15)** and column of gas **(12)**, etc. (column 3, lines 22-56). The size of the resulting particles may be controlled by the nozzle size, shape, type (not excluding those of the instant claims) as well as the working pressure and temperature in the column (column 3, lines 22-56). Figure 1 shows the apparatus for the production of gaseous microparticles. It is also disclosed that a resuspended solution of gaseous microparticles may be filtered immediately before injection into a

patient to increase the reliability (column 3, lines 60+; column 4, lines 13-15). The system/apparatus does not exclude a controller, such as a human for changing an operating parameter and the gaseous microparticles/bubble medium encompasses the gaseous microparticles/bubble medium of the instant claims and thus is capable of being generated for real time administration. Rossling et al. does not disclose a medium delivery system for direct injection into a patient or the production of microbubbles via ultrasound or the introduction of solid particles.

7. Evans, III et al. (US 5,885,216) discloses an apparatus for the injection of a contrast medium directly into a patient(s) (abstract; column 3, lines 4-8). The apparatus comprises a container holding a contrast medium **(10)**, a container holding a diluent **(11)**, an operator/controller and an electronic control system which provides for proper fluid flows according to the instructions of the operator (column 3, lines 57+; column 5, lines 63-66; figs 1 and 2). The operator tells the system the concentration desired, flow rate and total volume to be delivered (properties of the medium) for each phase of an injection where various constant flow rates during each phase may be utilized (column 6, lines 6-12). The metering pumps (peristaltic pump) **(12** and **13)** are used to draw contrast agent and diluent from the reservoirs (column 4, lines 30-45) where the mixture is then heated **(14** and **15)**, mixed with mixer **(20)** and a concentration monitor is used to provide feedback on the density, concentration, etc. (column 4, lines 44+; column 5, lines 4-11). Sensors/fluid assurance detectors **(22)** are used to inform the controller system when the container is empty or for fluid assurance to prevent the problem of air embolism (column 3, lines 63+; column 4, lines 3-15; column 5, lines 4-11). The

sensors of the disclosure encompass the sensors of the instant claims and are capable of the same properties, such as detecting a large amount of gas, etc. A "sterilizing filter" **(26)** is used to provide for sterile fluid coming out of the pump and to prevent migration of any bacteria from the patient into the pump and a spring-loaded ball valve is used to help prevent cross-contamination (column 4, lines 64+; column 5, lines 38-46). It is also a reasonable extension of the disclosure that more than two bulk containers may be used (column 8, lines 7-12).

8. Daum et al. (US 6,231,513) discloses a microbubble forming arrangement having a plurality of microholes which when a gas is passed through causes the gas to form numerous microbubbles in fluid (column 3, lines 1-6). The microbubble forming arrangement includes multi-perforated membrane (two dimensional material that includes microholes) or porous matrix (three dimensional structure which includes microholes) (column 3, lines 7-24). Daum et al. also discloses the use of piezoelectric ultrasound for the preparation of gas-filled microbubbles used for ultrasound diagnosis (column 4, lines 10-24).

9. Quay et al. (WO 96/40282) discloses the enhance production of gaseous microbubbles via the introduction of solid particles in the gas-liquid emulsion where there is a significant increase in bubble population per unit volume (abstract; p6, lines 7-12; p8, lines 7-25). The activation process of the disclosure provides for enhancement of the contrast in an ultrasound image generated during medical diagnosis (p4, lines 4-11).

10. At the time of the invention it would be obvious to one ordinarily skilled in the art to create the microparticles with the apparatus of Rossling et al. and administer them to a patient with the injector system of Evans, III et al. for direct administration of the contrast agent to a patient as both disclosures are drawn to the same utility, such contrast agents used for ultrasound imaging in a patient. The resulting combination of apparatus would lead to predictable results, such as the administration of the contrast agent with the correct concentration and minimized contrast waste (Evans, III et al. column 3, lines 25-32 and lines 43-56; column 6, lines 6-12). It would also be obvious to generate the microparticles via nucleation or piezoelectric ultrasound as they are known techniques in the art for generating gaseous microparticles with significant increase in bubble population per unit volume and thus enhanced imaging. One would have a reasonable expectation of success for introducing a plurality of gases via inlets in the apparatus of Evans, III et al. to vary/enhance the microbubble composition.

11. It is respectively pointed out that the instant claim 11 is a product-by-process limitation. Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed Cir. 1985). See MPEP 2113.

Response to Arguments

12. Applicant's arguments filed 3/9/09 have been fully considered but they are not persuasive.

13. Applicant asserts that Rossling et al. does not disclose a system whose controller is capable of real time control of the properties of the bubbles in a medium that is being prepared for real time administration into a patient.

14. The reference of Rossling et al. does not exclude a controller, such as a human who is capable of real time control of the properties of the bubbles, such as gas type where the introduction of a specific gas type via an inlet of the apparatus is controlled by a human operator.

15. Applicant asserts that Evans, III et al. teaches nothing about real time control/change of the properties of the bubbles in a medium for administration into a patient and into whom it can be immediately administered/injected.

16. Evans, III et al. teaches of a contrast medium apparatus in which the degree of concentration, flow rate or total volume (all encompassing the properties to be changed of the bubble medium) of the contrast medium administered can be continuously varied while the contrast medium is directly injected into a patient (Evans, III et al. column 3, lines 1-8; column 6, lines 6-12). For example, the operator/controller provides the instructions to the electronic control system for proper fluid flow (a property of the bubble medium) in real time (Evans, III et al. column 3, lines 57-63).

17. Applicant asserts that the size of the dried microparticles created by the method of Rossling et al. is entirely dependent on the size, shape and type of nozzle used in

their manufacture. Therefore, if the combined teaching of Rossling et al. and Evans, III et al. would certainly not yield a contrast dilution system in which the properties of the bubbles could be controlled real time and then administered immediately to a patient. Any change in microparticle size would require a different nozzle to be installed in the apparatus.

18. The instant claims do not require the real time change in size of the microparticles/bubble (i.e. property of the bubbles) but only that one property of the medium may be changed for real time administration.

19. Rossling et al. teaches of the preparation of microparticles/bubble medium and Evans, III et al. teaches of the preparation of the contrast medium with the desired concentration via mixing of contrast agent/microparticles and diluent. It would have been obvious to one skilled in the art to attach the apparatus of Rossling et al. and Evans, III et al. in series to directly transfer the microparticles/bubble medium of Rossling et al. into the apparatus of Evans, III et al. for the direct injection into a patient. Evans, III et al. teaches that the degree of concentration (a property of the bubble medium) of the contrast medium can be continuously varied while the contrast medium is directly injected into a patient.

20. Applicant asserts that Daum et al. discloses devices that are inserted into a blood vessel wherein they are used to form microbubbles in the blood for use in ultrasonic imaging procedures and another device features a needle of which is affixed a piezoelectric ultrasound transmitter.

21. Daum et al. does teach of the preparation of microbubbles via passing gas through a microbubble forming arrangement having a plurality of microholes to form numerous microbubbles in fluid and to attach a piezoelectric ultrasound transmitter to the microbubble forming arrangement to break the flow of gas into microbubbles in fluid. Therefore it would have been obvious to one skilled in the art to use a microbubble forming arrangement having a plurality of microholes (i.e. tube structures) (Daum et al. column 2, lines 52-67) with an attached piezoelectric ultrasound transmitter to form numerous microbubbles in fluid in the apparatus of Evans, III et al. as they are both drawn to the same utility, such as the preparation of microbubbles.

22. Applicant asserts that Quay et al. is not capable of creating and hence altering the characteristics of the bubbles on the fly, as the demands of the medical procedure change.

23. The reference of Quay et al. was not use to teach of altering the characteristics of the bubbles on the fly but used to teach of the inclusion of solid particles in a gas-liquid emulsion which provides a significant increase in bubble population per unit volume and thus enhancement of the contrast in an ultrasound image generated during medical diagnosis. Therefore it would have been obvious to one skilled in the art to include solid particles in the gas-liquid emulsion of Rossling et al. to provide a significant increase in bubble population per unit volume. Evans, III et al. teaches that the degree of concentration of the contrast medium (a property of the bubble medium) can be continuously varied while the contrast medium is directly injected into a patient. Thus,

the alteration of at least one property of the medium (i.e. degree of concentration of the contrast medium) may be changed for real time administration.

New grounds of rejection

Claim Rejections - 35 USC § 112

24. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

25. Claim 40 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The recitation of a "first member and second member" is confusing and unclear as there are no structural properties for the first and second members provided in the disclosure.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/
Examiner, Art Unit 1618